

CLAIMS

What is claimed is:

1. A matrix for treating a patient having degenerative disc disease, the matrix comprising

an injectable fluid comprising digestion-resistant remodelable collagen, said collagen being cross-linked through photooxidative catalysis and irradiation by visible light; and

a plurality of living cells dispersed within said injectable fluid to form an injectable cell matrix for treating degenerative disc disease, said cells having inherent capability to elaborate proteoglycans *in vivo*.

2. The injectable matrix of claim 1, further comprising

a plurality of purified cell growth factors dispersed within said injectable cell matrix to form an injectable disc regeneration fluid, said living cells being responsive to said purified cell growth factors by increased elaboration of proteoglycans *in vivo*.

3. The matrix of claim 1 wherein said cells are chondrocytes.

4. The matrix of claim 1 wherein said cells are mesenchymal stem cells.

5. The matrix of claim 4 wherein said cells are human-derived.

6. The matrix of claim 1 wherein said collagen is cross-linked using methylene blue as a photooxidative catalyst.

7. The matrix of claim 1 wherein said cells are cultured *in vitro* to increase their response to said cell growth factors.

8. The injectable disc regeneration fluid of claim 2 wherein at least two of said plurality of cell growth factors are bone-derived.

9. An injectable disc regeneration fluid, comprising
an injectable cell matrix according to claim 7; and
a plurality of cell growth factors dispersed within said injectable cell matrix to
form an injectable disc regeneration fluid, said living cells being
responsive to said cell growth factors by increased elaboration of
proteoglycans *in vivo*.
10. A method of treating a patient presenting with degenerative disc disease, the
method comprising
providing an injectable disc regeneration fluid according to claim 2; and
injecting said injectable disc regeneration fluid into at least one of said
patient's intervertebral discs to treat degenerative disc disease in said
disc.
11. A method of continuing treatment of a patient presenting with degenerative disc
disease, the method comprising
treating the patient according to the method of claim 10; and
injecting a plurality of cell growth factors into said at least one of said
patient's intervertebral discs after completion of the method of claim
10 to continue treatment of a patient presenting with degenerative disc
disease.
12. A patient having a history of degenerative disc disease, wherein the patient has
been treated by the method of claim 11.
13. An intervertebral disc *in vivo*, said disc having been injected with injectable disc
regeneration fluid according to claim 2.
14. A method of treating a patient presenting with signs of hydrodynamic
intervertebral disc dysfunction, the method comprising

diagnosing hydrodynamic disc dysfunction in at least one intervertebral disc of
said patient;
5 testing said at least one intervertebral disc of said patient to establish cellular
proteoglycan production within said at least one disc; and
injecting a plurality of purified cell growth factors into said at least one disc to
treat a patient presenting with signs of hydrodynamic intervertebral
disc dysfunction.

15. The method of claim 14 wherein at least two of said plurality of cell growth
factors are bone-derived.

16. An injectable cell growth medium for intervertebral disc regeneration, said
medium comprising

an injectable fluid comprising digestion-resistant remodelable collagen, said
collagen being cross-linked through photooxidative catalysis and
5 irradiation by visible light; and
a plurality of purified cell growth factors dispersed within said fluid to form an
injectable cell growth medium.

17. The injectable cell growth medium of claim 16 wherein at least two of said
plurality of cell growth factors are bone-derived.

18. An injectable disc regeneration fluid for intervertebral discs, the material
comprising

injectable cell growth medium according to claim 17; and
cells responsive to said injectable cell growth medium through proteoglycan
5 elaboration *in vivo*.

19. The disc regeneration fluid of claim 18 wherein said cells are chondrocytes.

20. The disc regeneration fluid of claim 18 wherein said cells are mesenchymal stem
cells.

21. The disc regeneration fluid of claim 20 wherein said cells are human-derived.
22. The disc regeneration fluid of claim 20 wherein said cells are cultured *in vitro* to increase their response to said cell growth factors.
23. An injectable material for treating a patient for hydrodynamic disc dysfunction, the material made by a process comprising
- cross-linking collagen through photooxidative catalysis and irradiation by visible light;
- 5 purifying a plurality of bone-derived cell growth factors;
- dispersing said purified bone-derived cell growth factors within said cross-linked collagen; and
- dispersing cells responsive to said purified plurality of bone-derived cell growth factors within said cross-linked collagen to form an injectable
- 10 material for treating hydrodynamic disc dysfunction.
24. The injectable material of claim 23 wherein said cells are chondrocytes.
25. The injectable material of claim 23 wherein said cells are mesenchymal stem cells.
26. The injectable material of claim 24 wherein said cells are human-derived.
27. The injectable material of claim 24 wherein said cells are cultured *in vitro* to increase their response to said cell growth factors.
28. A method of hydrating an intervertebral disc annulus fibrosus *in vivo*, the method comprising
- testing said disc for cellular proteoglycan production within said disc; and
- injecting cell growth medium according to claim 16 into said disc to hydrate
- 5 the annulus fibrosus.

29. A method of reducing susceptibility to herniation of an intervertebral disc in a patient having a history of intervertebral disc herniation, the method comprising testing said disc for cellular proteoglycan production within said disc; and injecting cell growth medium according to claim 16 into said disc to reduce
5 susceptibility to herniation through hydration of the annulus fibrosus.
30. A method of increasing the height of a patient presenting with hydrodynamic disc dysfunction in at least one intervertebral disc, the method comprising testing said at least one disc for cellular proteoglycan production within said at least one disc; and
5 injecting cell growth medium according to claim 16 into said at least one disc to increase the height of said patient by increasing intervertebral spacing through increased proteoglycan production in said at least one disc.
31. An injectable cell suspension for treating a patient having degenerative disc disease, the suspension comprising an injectable fluid comprising a plurality of purified cell growth factors; and a plurality of living cells dispersed within said injectable fluid to form an
5 injectable cell suspension for treating degenerative disc disease, said cells being responsive to said cell growth factors by increased elaboration of proteoglycans.
32. The injectable cell suspension of claim 31 wherein said cells are chondrocytes.
33. The injectable cell suspension of claim 31 wherein said cells are mesenchymal stem cells.
34. The injectable cell suspension of claim 33 wherein said cells are human-derived.

35. The injectable cell suspension of claim 31 wherein said cells are cultured *in vitro* to increase their response to said cell growth factors.

36. The injectable cell suspension of claim 31 wherein at least two of said plurality of cell growth factors are bone-derived.

37. A method of treating a patient presenting with degenerative disc disease, the method comprising

providing an injectable cell growth medium according to claim 16; and

injecting said injectable cell growth medium into at least one of said patient's

5 intervertebral discs to treat degenerative disc disease in said disc.

38. A method of treating a patient presenting with hydrodynamic disc dysfunction, the method comprising

providing an injectable material according to claim 23; and

injecting said injectable material into at least one of said patient's

5 intervertebral discs to treat hydrodynamic disc dysfunction in said disc.

39. A method of treating a patient presenting with degenerative disc disease, the method comprising

providing an injectable cell suspension according to claim 31; and

injecting said injectable cell suspension into at least one of said patient's

5 intervertebral discs to treat degenerative disc disease in said disc.

40. A method of cross-linking collagen to make digestion-resistant remodelable cross-linked collagen, the method comprising

providing a hydrogel comprising collagen;

containing said hydrogel within a semipermeable membrane, said membrane

5 being substantially transparent to visible light and substantially

permeable to at least one photooxidative catalyst;

transporting at least one photooxidative catalyst through said semipermeable

membrane and into said hydrogel; and

irradiating said hydrogel with visible light to cross-link said collagen.

41. The method of claim 40 comprising an additional step between said containing step and said transporting step, the additional step being

submerging said hydrogel-containing semipermeable membrane in a high salt:high sucrose solution for about 24 to about 72 hours.

42. The method of claim 41 wherein said hydrogel comprises nucleus pulposus tissue.

43. The method of claim 42 wherein said transporting step occurs at a substantially constant hydrogel temperature of about 10°C.

44. Digestion-resistant remodelable cross-linked collagen made by the method of claim 43.

45. The method of claim 41 wherein said hydrogel comprises substantially Type II collagen.

46. The method of claim 43 wherein said semipermeable membrane comprises dialysis tubing having a molecular weight cutoff of about 3500 Daltons.

47. The method of claim 43 wherein said transporting step and said irradiating step are substantially simultaneous.

48. The method of claim 43 wherein said transporting step occurs while said semipermeable membrane containing said hydrogel is immersed in a solution comprising at least one photooxidative catalyst.

49. The method of claim 43 comprising an additional step after said irradiating step, the additional step being

terminating said transporting step and said irradiating step when said collagen cross-linking is substantially complete.

50. The method of claim 49 comprising an additional step after said terminating step, the additional step being
extracting said cross-linked collagen from said hydrogel.
51. The method of claim 43 wherein said at least one photooxidative catalyst comprises methylene blue.
52. A fluid matrix for treating intervertebral disc disease in a vertebrate, said fluid comprising nucleus pulposus tissue of a donor vertebrate.
53. The fluid matrix of claim 52 wherein said nucleus pulposus tissue is cross-linked.
54. The fluid matrix of claim 53 further comprising a growth factor.
55. The fluid matrix of claim 54 further comprising a plurality of living cells.
56. The fluid matrix of claim 55, wherein said plurality of living cells comprise chondrocytes.
57. The fluid matrix of claim 55, wherein said plurality of living cells comprise mesenchymal stem cells.
58. The fluid matrix of claim 55, wherein said plurality of living cells are human-derived.
59. The fluid matrix of claim 52, wherein said nucleus pulposus tissues are decellularized.